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Case Report

A case report of pregnancy after fertility-sparing treatment for endometrial cancer in young women

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Abstract

Introduction: The incidence of endometrial cancer (EC) among young women has been increasing. The standard treatment for EC is surgical; however, fertility-sparing treatment options are available for young women with stage IA, grade 1 disease who wish to preserve their fertility. After treatment, pregnancy should be attempted as soon as possible following successful endometrial remission. If necessary, assisted reproductive technology should be actively considered to improve pregnancy rates. The limited time window between disease remission and recurrence makes in vitro fertilization (IVF) a favorable option for achieving pregnancy in the short term. IVF has been shown to be effective in reducing treatment duration for EC patients.

Case Report: We present a case of pregnancy in a young woman after fertility-sparing treatment for endometrial cancer. Conservative management consisted of a six-month course of GnRH-a and MPA, during which hysteroscopic evaluation was performed to assess the therapeutic response. Following this, the patient underwent IVF to increase her chances of conception and ultimately achieved pregnancy through oocyte donation. The pregnancy was complicated by multiple adverse events; however, the patient successfully delivered a live newborn.

Conclusion: Fertility-preserving treatments for young women with endometrial cancer improve reproductive outcomes. Careful patient selection and a multidisciplinary approach are essential for achieving favorable results.

Keywords: Endometrial carcinoma, fertility-sparing treatment, in vitro fertilization, pregnancy

Introduction

Endometrial cancer (EC) is the second most common gynecological malignant cancer. Notably, there has been a rising trend in the incidence of EC among younger patients, with around 5% of cases reported in women under the age of 40 [1-3]. Endometrioid adenocarcinoma EMC and AEH is a hysterectomy is the main pathological and histological type of EC, and atypical endometrial hyperplasia (AEH) is considered a precursor of EMC. The primary treatment for EC and AEH is a hysterectomy. In the case of EMC, a bilateral salpingo-oophorectomy may also be necessary, with or without regional lymphadenectomy. For young patients diagnosed with stage Ia, Grade 1 (G1) EMC, fertility-sparing treatments (FSTs) are suitable options[3-6]. In general, there are several different types of treatments, including high doses of medroxyprogesterone acetate (MPA), megestrol acetate (MA), and gonadotropin-releasing hormone agonists (GnRHa). A levonorgestrel-releasing intrauterine device (LNG- IUD) is also used to treat AEH and EMC, alone or in combination with oral progestins and GnRHa [3]. In young patients with earlystage EMC and AEH, letrozole combined with GnRHa is also an option [7].

The pregnancy rate after FSTs has been reported to be approximately 18–34 % [3]. Gynecologists who treat these patients play a crucial role in encouraging them to achieve pregnancy as early as possible after FST. Assisted reproductive technologies (ART) significantly facilitate this process.

We present a case of pregnancy achieved through in vitro fertilization following conservative treatment for EC, emphasizing the clinical considerations and challenges related to fertility preservation in this patient population.

Case Presentation

The patient's history

A 38-year-old patient was diagnosed with EC through hysteroscopic biopsy performed in November 2019. Her medical history was notable for uterine fibroids and a prior myomectomy performed four years earlier. At the time of diagnosis, she was trying to conceive.

Prior to hysteroscopy, the patient experienced intermenstrual bleeding on several occasions. Gynecological examination and transvaginal ultrasound revealed a suspected thickened endometrium. During hysteroscopy, several polypoid formations up to 5mm in size were observed within the uterine cavity, and the endometrium appeared thickened. The histopathological examination suggests the presence of a well-differentiated adenocarcinoma with predominantly endometrioid differentiation. The carcinoma is characterized by pseudopolypoid fragments and focal papillary architecture, mild nuclear atypia, and an absence of vascular invasion. Immunohistochemical staining was performed, and the following results were observed: Vimentin positive (+), Estrogen positive (+), Progesterone positive (+), p16 focally positive (+), CEA negative (-).The patient subsequently underwent magnetic resonance imaging (MRI) to exclude metastatic disease.

Given the patient's young age and desire to preserve fertility, conservative

management was chosen, consisting of a six-month course of GnRH-a and MPA. Three months after initiation of therapy, the patient underwent repeat hysteroscopy to assess the therapeutic response. During this procedure, a 0.8mm endometrial polyp was identified anterior to the ostium of the right uterine tube. Histopathological examination confirmed the presence of an endometrial polyp without evidence of malignancy.

The patient continued GnRH/MPA therapy and, after an additional three months, underwent another routine hysteroscopic endometrial evaluation. Postoperative histopathology demonstrated complete regression, with no evidence of carcinoma or atypical endometrial hyperplasia.

IVF treatment and pregnancy outcome

After completion of fertility-sparing therapy, the patient was 39 years old and expressed a desire to achieve pregnancy as soon as possible. Controlled ovarian stimulation (COS) was therefore planned, with a LNG-IUD used as maintenance therapy following fertility-sparing treatment.

Prior to initiation of the COS cycle, the patient's endometrial status was assessed by gynecologic oncologists and reproductive medicine specialists. The LNG-IUD was placed during hysteroscopic evaluation, in July 2020.Baseline serum hormone levels, including follicle-stimulating hormone, luteinizing hormone, estradiol, and progesterone, were measured. Ovarian reserve was assessed by serum anti-Müllerian hormone (AMH), which was 1,27ng/mL. A shortantagonist protocol with hMG (Menopur) was selected for COS, and ovulation was triggered with a subcutaneous injection of recombinant human chorionic gonadotropin.A total of six oocytes were retrieved following controlled ovarian stimulation. Five oocytes were at the metaphase II (MII) stage and were inseminated by conventional IVF. Normal fertilization was observed in four oocytes, while one oocyte showed degeneration. Three blastocysts were cryopreserved and subsequently used in three frozen embryo transfer (FET) cycles.

After completion of oocyte retrieval and subsequent embryo culture, the LNG-IUD was removed, and the endometrium was re-evaluated. Following hysteroscopic confirmation of the absence of pathological endometrial carcinoma or atypical endometrial hyperplasia, FET was performed. Despite three FET attempts after device removal, no pregnancy was achieved. The patient was subsequently counseled regarding alternative reproductive options, including in vitro fertilization with oocyte donation. This procedure was performedin April 2024and in May 2024, the patient achieved a twin pregnancy. Unfortunately, one of the twins was diagnosed with a central nervous system anomaly, and selective fetal reduction was performed after approval by the institutional ethics committee. At 25 weeks of gestation, premature rupture of membranes occurred in the remaining twin, complicated by chorioamnionitis, necessitating delivery. Cesarean section was performed at 28 weeks of gestation, in December 2024, and the newborn was transferred to the Neonatology Institute for further care and treatment.

Follow-up Evaluation

At five months postpartum, the patient underwent diagnostic hysteroscopy with fractional exploratory curettage as part of follow-up evaluation. Histopathological analysis revealed a normal finding, without atypia or dysplasia. Following the results, the patient continued to attend regular follow-up visits.

Discussion

The incidence of EC among young women has been increasing. The standard treatment for EC consists of total extrafascial hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymph node assessment to optimize survival outcomes [8]. However, for young women with stage IA, grade 1 disease who wish to preserve fertility, fertility-sparing treatment options are available. As a result, there has been a growing focus on conservative management approaches that enable eligible patients to conceive after undergoing treatment.

Several fertility-sparing treatment modalities have been described, including high-dose of MPA, MA, and GnRH-a. The LNG-IUD is also widely used in the treatment of AEH and early-stage EC, either alone or in combination with oral progestins and GnRH-a [3]. GnRH-a has demonstrated beneficial effects not only in fertility preservation during EC treatment but also in facilitating ovarian stimulation and embryo implantation during subsequent assisted reproductive procedures. Regular endometrial surveillance, including hysteroscopic evaluation every 3–6 months, is mandatory during progestin therapy [7,8]. In selected young patients with early-stage EC or AEH, aromatase inhibitors such as letrozole combined with GnRH-a may also represent a therapeutic option [9].

The initial response rate of early EC patients after progesterone application is 60–80%. Given the high risk of recurrence (25–40%) and the relatively short disease-free interval (12–28 months) following treatment [10, 11], it is recommended that pregnancy be pursued as soon as possible after achieving successful endometrial remission. ART should be actively considered, if necessary, to improve pregnancy rate [12]. The limited time window between disease remission and recurrence makes IVF a favorable option for achieving pregnancy in the short term. IVF has been proven to be effective in reducing treatment duration for EC patients (13). Recent studies have demonstrated that women who undergoing IVF have better pregnancy outcomes than those who conceive naturally [14,-16]. Gallos et al. reported that the live birth rates for AEH and EC patients were 26.3% and 28% respectively, and the pregnancy rate with ART was higher than that of natural conception (39.4% vs 14.9%) [17].

In this case report, controlled ovarian stimulation was initiated immediately after complete remission to minimize the interval between disease remission and potential recurrence. A LNG-IUD was applied during COS to protect the endometrium from elevated estrogen levels that may promote disease progression.A study of female patients pursuing either social oocyte cryopreservation or oocyte donation showed that the use of LNG-IUDs during COS had no apparent negative impact on cycle performance, including total oocytes, mature oocytes, clinical pregnancy rate, and live birth rate [18]. Yin et.al reported a total recurrence rate of 23.9% in 67 patients with EEC/AEH after COS and compared with patients who did not use LNG-IUD during COS, the recurrence rate was lower in the group that used LNG-IUD(12.1% vs. 35.3%). In this study from one tertiary hospital in China based on 10 year experience showed that patients with early stage EMC and AEH treated with assisted reproductive technology after FSTs might benefit from LNG-IUDs present during COSand the use of LNG-IUD during COS was a favorable factor for better oncologic outcomes after COS [19].

In this case, the pregnancy was complicated by multiple adverse events; however, the patient ultimately delivered a live newborn. The remaining twin was born alive at 28 weeks of gestation, requiring neonatal intensive care. Most patients decide for definitive hysterectomy after the birth of their first child in order to reduce the risk of disease recurrence. Nevertheless, the literature also reports cases of consecutive live births following fertility-sparing treatment for endometrial carcinoma [20].

Conclusion

Fertility-preserving treatment options for young patients with endometrial cancer have significantly improved their chances of achieving reproduction. However, careful selection of patients who are suitable for this type of treatment, as well as the involvement of a multidisciplinary medical team in their follow-up and definitive management, is essential for a favorable outcome and good prognosis.

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